The interactive web-based histology atlas system

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Molecular pathways and mechanisms underlying human cancer are frequently investigated in animal models. Studies to identify and dissect molecular pathways include the discovery of genes and their subsequent analysis in transgenic and 'knock-out' mice. A critical aspect in such investigations is the evaluation of organ integrity and histology upon the alteration or inactivation of specific genes. Results from such studies are usually published in scientific journals. However, due to print space and costs the display of large high quality images is limited. Furthermore, the printed media does not permit an easy comparison of histological images published in different journals and different years. The Internet provides a tool for the timely and inexpensive dissemination of scientific data to the research community. However, its potential for the analysis of histological images has not been explored. Here we present a web-based interactive histology atlas (http://histology.nih.gov) that permits the retrieval of annotated, high-resolution histology images via the Internet. This histology atlas also takes advantage of the interactive nature of the Internet to support the communication between different research groups. As an outline forum this atlas provides the framework to evaluate and understand cancer pathology, and to develop a consensus between veterinary and human pathologists. *Oncogene* (2000) **19,** 989–991.

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Introduction

The histology atlas provides histology images from animal and human tissues via the Internet. These images are cataloged in a database, with liberal annotations to guide researchers through key aspects of the images. The atlas acts as a forum for continuing consensus building between veterinary and human cancer communities, with on-line bulletin boards and chat rooms.

The design of the histology atlas is user friendly and permits future additions and performance enhancements. It is based on client-server, 'three-tier' software architecture to improve performance of image retrieval and presentation to the end user. Three-tier architecture systems are based on three elements: clients, middle-ware and servers. The histology atlas client is any common HTML 4.0 (ISO 8879:1986) web browser on any personal computer running Windows, Macintosh or Unix connected to the Internet. The user selects search criteria via a form on the search page of the histology atlas (http://histology.nih.gov/) (Figure 1). Upon submission, the form is passed to the remote middle-ware written in Tango™, a development product of Pervasive Software, Inc.

The middle-ware passes the selected criteria into data tokens, and formats these into a query. The middle-ware then queries the server, which is a structured query language database (SQL ISO/IEC 9075:1992). The SQL database retrieves any matching database records and passes these results back to the middle-ware (Figure 2). The middle-ware responds to the user with formatted, custom web pages, based on the results, which include thumbnails of the target images, and the opportunity for the user to narrow the search criteria. Once the user has selected the histology they wish to examine, the middleware will send an interactive page with scientific details and an interactive Java™ Applet (Figure 3).

The dimensions of the image files are at least 1400×1000 pixels. Such files, with compression, are at least 2 MB in size each. These images require 1–5 min to transfer via the Internet depending on the client's Internet connection. In the histology atlas, transfer speed is improved but the image is initially reduced to 30%. Using the Java™ Applet the user can select regions of interest (ROI's) in the image and magnify these regions up to original size. The middleware retrieves only the ROI. Following these steps the size of the data transfers are significantly reduced, and speed is increased. Additional text information is also provided and linked to external sources such as the National Library of Medicine and the Jackson Laboratory whenever possible.

A deceptively powerful feature of the histology atlas is the on-line submission system. Contributors are asked to submit their images and annotations via a web page. This eliminates the inherent problems with mailing disks or actual slides.

Maintenance is also handled via the Internet, and with the growing speed and capacity of Information Technology, the ease of use of the system will improve relatively quickly.

Communication tools

The atlas will act as forum for continuing consensus building between veterinary and human cancer communities, with on-line editing forms, bulletin

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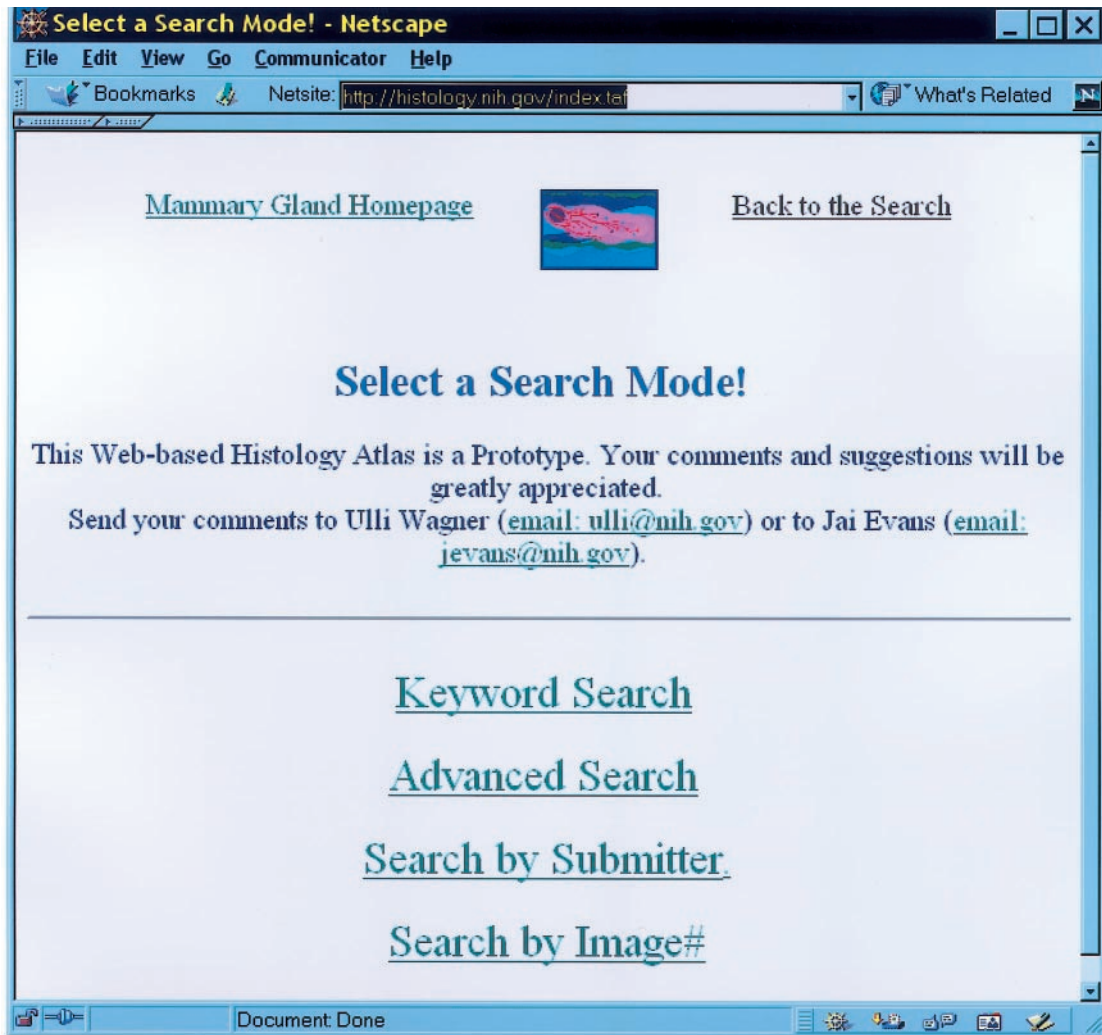
Figure 1 Introductory search page

boards and chat rooms. Specifically, the submitting researcher can update or correct the information associated with images via a web form. In addition, there is an electronic bulletin board for general comments and a bulletin and a bulletin board for each of the images.

In the near future dual-station client software will be installed that allows different researchers to evaluate any image simultaneously. While one researcher will control the view of the image, the second researcher will see the changes on their client machine.
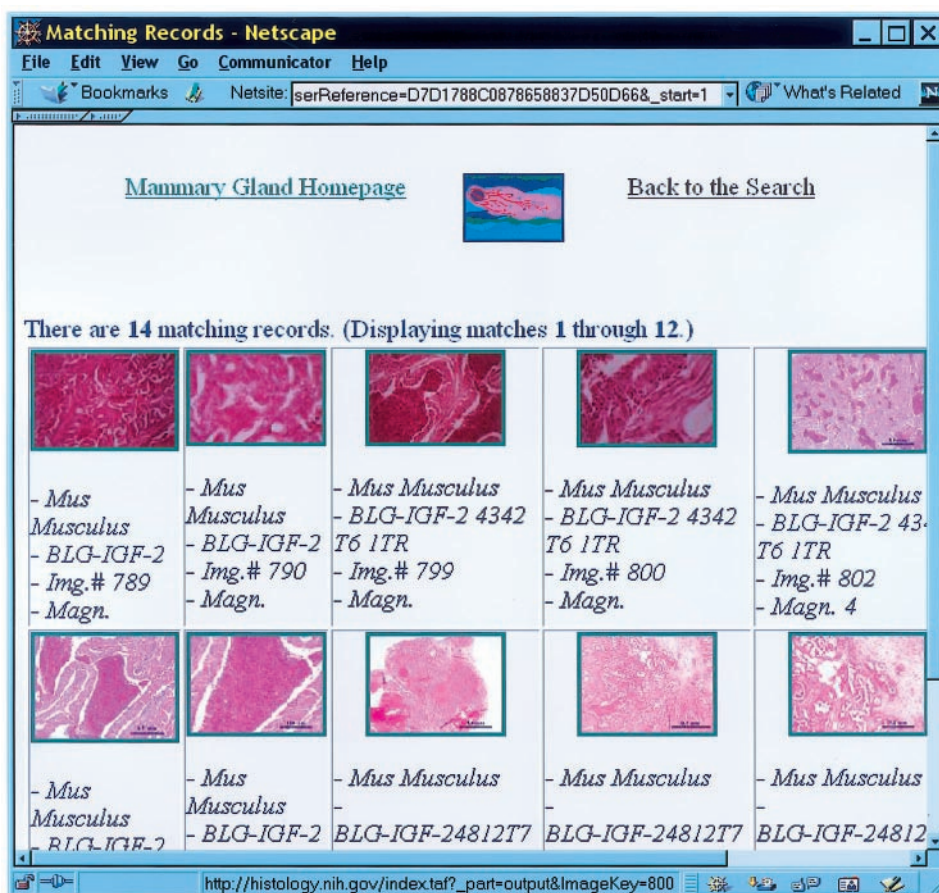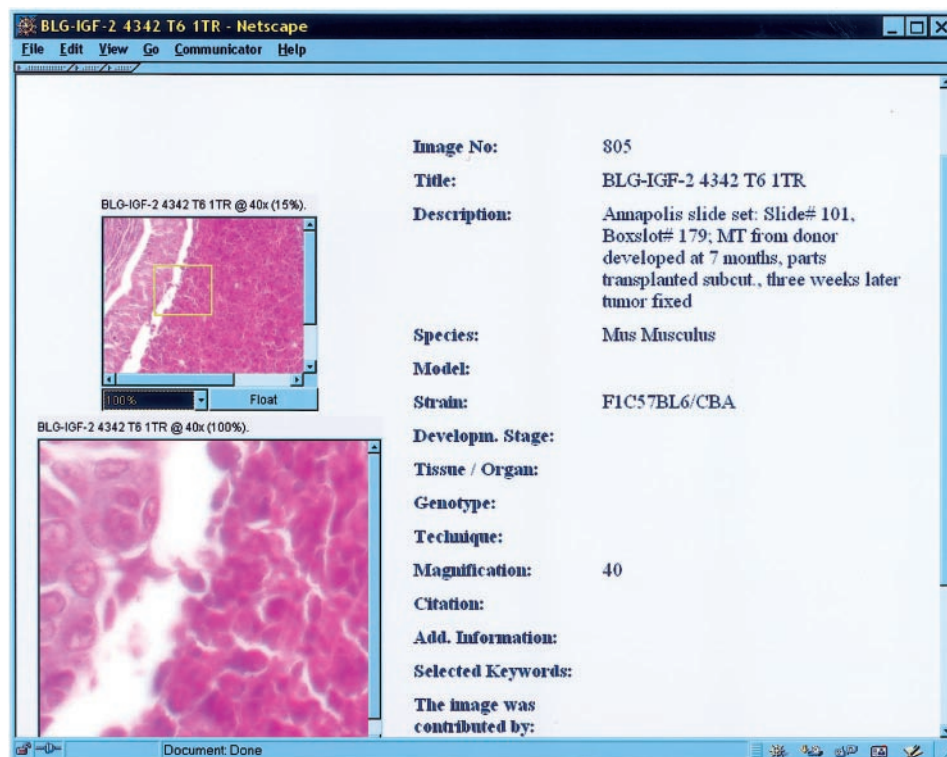
Figure 2 Thumbnail search results

Figure 3 Interactive Applet and annotations